

REMARKS

Claims 1-4, 6, and 11 constitute the pending claims in the present application. Applicants cancel, without prejudice, claim 11. Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Before addressing the issues raised by the Examiner in the previous Office Action and the previous Advisory Action, Applicants note that Applicants' amendments to the claims are fully supported by the specification (see, for example, page 5, line 29 – page 6, line 3; page 16, lines 9-19; page 17, lines 17-19; page 17, line 29-page 18, line 15). No new matter has been entered.

1. Applicants note that the amendments put forth on February 2, 2004 have been entered in full. Applicants note with appreciation that the drawings submitted on February 2, 2004 have been accepted.
2. Claims 1, 2, 4, 6, and 11 are rejected under 35 U.S.C. 112, second paragraph, as indefinite for allegedly failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. Applicants traverse this rejection and contend that the rejection is moot in light of the amended claims.

Applicants contend that, at the time of filing of the present application, the term "hedgehog polypeptide" was well known and readily understood in the art. In addition to the references cited in the specification and the references cited by the Examiner, Applicants contend that at the time of filing of the instant application well over 1000 papers on the topic had been published. Accordingly, one of skill in the art can readily appreciate the meaning of the term "hedgehog polypeptide" and can readily refer to the literature or to web-based sequence resources such as GenBank to elucidate the nucleic acid or amino acid sequence of a hedgehog polypeptide.

Nevertheless, to expedite prosecution, Applicants have amended the claims to more particularly point out that the hedgehog polypeptides for use in the presently claimed methods are hedgehog polypeptides comprising the sequence of a naturally-occurring, mammalian Sonic hedgehog polypeptide, or N-terminal autoproteolytic fragment thereof. Applicants' amendments

are not in acquiescence to the rejection, and Applicants reserve the right to prosecute claims of similar or differing scope. Reconsideration and withdrawal of this rejection is respectfully requested.

3. Claims 1-4, 6, and 11 are rejected under 35 U.S.C. 112, first paragraph, for allegedly failing to enable one of skill in the art to practice the claimed invention. Applicants traverse this rejection and contend that the rejection is moot in light of the amended claims.

Applicants contend that the previously pending claims were enabled throughout their scope. Nevertheless, to expedite prosecution, Applicants have amended the claims to more particularly point out the hedgehog polypeptides for use in the methods of the present invention. Specifically, the hedgehog polypeptides for use in the methods of the present invention are naturally occurring, Sonic hedgehog polypeptides, or N-terminal autoproteolytic fragments thereof. Exemplary mammalian Sonic hedgehog polypeptides are described in detail in the application (See, for example, Table 1). Applicants' amendments are not in acquiescence of the rejection, and Applicants reserve the right to prosecute claims of similar or differing scope. Reconsideration and withdrawal of this rejection are respectfully requested.

4. Claims 1-4, 6, and 11 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over U.S. Patent No. 5884079 (Ingham et al.) in view of Molses et al. Applicants traverse this rejection and contend that the rejection is moot in light of the amended claims.

The combination of Ingham et al. and Molses et al. was previously cited by the Examiner as allegedly rendering the claimed invention obvious. Applicants respectfully disagree with any allegation that the broad teachings of Ingham et al. in combination with the teachings of Molses et al. undermine the patentability of the presently claimed invention.

Applicants contend that a valid patent may issue for a nonobvious species related to a prior patented invention, even though the improvement falls within the disclosure of that prior patent. A prior genus which **does not explicitly** disclose a species does not anticipate a later claim to that species. This position is well supported by the holdings of the Federal Circuit. See, for example, *Corning Glass Works v. Sumitomo Electric U.S.A.*, 868 F.2d 1251, 1262, 9 USPQ2d 1962, 1970 (Fed. Cir. 1989).

Applicants contend that the relationship between the pending claims and the cited art is largely analogous to the factual situation in the above example. Applicants assert that the presently claimed invention provides a particular combination of elements and constitutes a species. Applicants' species is unobvious and patentable over the generic teachings of Ingham et al. because Ingham et al., even when taken in combination with Molses et al., fail to either teach or suggest the particular combination of elements recited in the pending claims.

The combination of Ingham et al. and Molses et al. fail to teach the benefits of the particular combinations of elements set forth in the pending claims. Specifically, these references provide no motivation to select the particular hedgehog polypeptides, the particular modified hedgehog polypeptides, and the particular method of use set forth in the pending claims. That is, although Ingham et al. broadly teach methods and compositions using *hedgehog* polypeptides, and although Molses et al. provide motivation to test NGF for its efficacy in neuronal tissue, the combination of references provides no motivation to specifically select the particular hedgehog polypeptides, lipophilic modifications, or the particular method of use, as presently claimed. MPEP 2144.08 outlines the guidelines for determining that a reference renders an invention obvious and directs the Examiner to "determine whether one of ordinary skill in the relevant art would have been motivated to make the claimed invention as a whole, i.e., to select the claimed species or subgenus from the disclosed prior art genus."

In the previous Advisory Action, the Examiner indicated that the proposed claims, if entered, would not overcome the rejection under 35 U.S.C. 103(a) because hedgehog polypeptides made in COS cells according to Ingham et al. are post-translationally modified. Applicants note that hedgehog polypeptides obtained directly from mammalian cells (mammalian cells that are producing such polypeptides) are modified on both the N-terminal amino acid residue and on the C-terminal amino acid residue (of the N-terminal autoproteolytic fragment). This modified form of the polypeptide (e.g., a polypeptide modified with a fatty acid on the N-terminus and a cholesterol on the C-terminus) is the active form produced by the mammalian cells. In contrast, the modified hedgehog polypeptides for use in the methods of the present invention are modified only on the N-terminal amino acid residue.

Applicants maintain that Ingham et al. and Molses et al. fail to satisfy the criteria necessary for rendering obvious Applicants' invention. The MPEP and a substantial body of case law clearly recognize the patentability of a species despite the presence of prior art to the genus, as is the case here. Accordingly, the claimed invention is patentable in light of the prior art, and reconsideration and withdrawal of this rejection is respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945, under Order No. CIBT-P01-098.**

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Respectfully Submitted,



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